Polycyclic [2+3]-Cycloadducts from the Thermal Decomposition of Bis(2,5-dihydro-1,3,4-thiadiazoles) in the Presence of N-Methylmaleimide

Mlostoń, Grzegorz ; Celeda, Malgorzata ; Linden, Anthony ; Heimgartner, Heinz

Abstract: Thermal decomposition of a mixture of the two stereoisomeric bis(2,5-dihydro-1,3,4-thiadiazoles) cis- and trans-2, which was prepared by treatment of 2,2,4,4-tetramethylcyclobutane-1,3-dithione with excess of diazomethane in the presence of two equivalents of N-methylmaleimide, led to a mixture of three 1:2 cycloadducts of type 4. The structures of these thiocarbonyl methanide-adducts have been established by X-ray crystallography. In the presence of only one equivalent of N-methylmaleimide, a complex mixture of the three 1:2 adducts of type 4, the known dispirocyclic bis-thiiranes cis- and trans-3, and a 1:1 adduct 6, containing one thiirane ring and one fragment resulting from a [2+3]-cycloaddition of a thiocarbonyl methanide, was formed. The structure of the latter has again been proven by X-ray crystallography.

Polycyclic [2+3]-Cycloadducts from the Thermal Decomposition of Bis(2,5-dihydro-1,3,4-thiadiazoles) in the Presence of *N*-Methylmaleimide

by G. Mloston[1*], M. Celeda[1], A. Linden[2] and H. Heimgartner[2*]

[1]*Section of Heteroorganic Compounds, University of Lódz, Narutowicza 68, PL-90-136 Lódz, Poland*

[2]*Institute of Organic Chemistry, University of Zürich, Winterthurerstrasse 190, CH-8057 Zürich, Switzerland*

Thermal decomposition of a mixture of the two stereoisomeric bis(2,5-dihydro-1,3,4-thiadiazoles) *cis*- and *trans*-**2**, which was prepared by treatment of 2,2,4,4-tetramethylcyclobutane-1,3-dithione with excess of diazomethane in the presence of two equivalents of *N*-methylmaleimide, led to a mixture of three 1:2 cycloadducts of type **4**. The structures of these thiocarbonyl methanide-adducts have been established by X-ray crystallography. In the presence of only one equivalent of *N*-methylmaleimide, a complex mixture of the three 1:2 adducts of type **4**, the known dispirocyclic bis-thiiranes *cis*- and *trans*-**3**, and a 1:1 adduct **6**, containing one thiirane ring and one fragment resulting from a [2+3]-cycloaddition of a thiocarbonyl methanide, was formed. The structure of the latter has again been proven by X-ray crystallography.

Key words: thiocarbonyl ylides, 1,3-dipolar cycloaddition, tetrahydrothiophenes, 2,5-dihydro-1,3,4-thiadiazoles, crystal structure

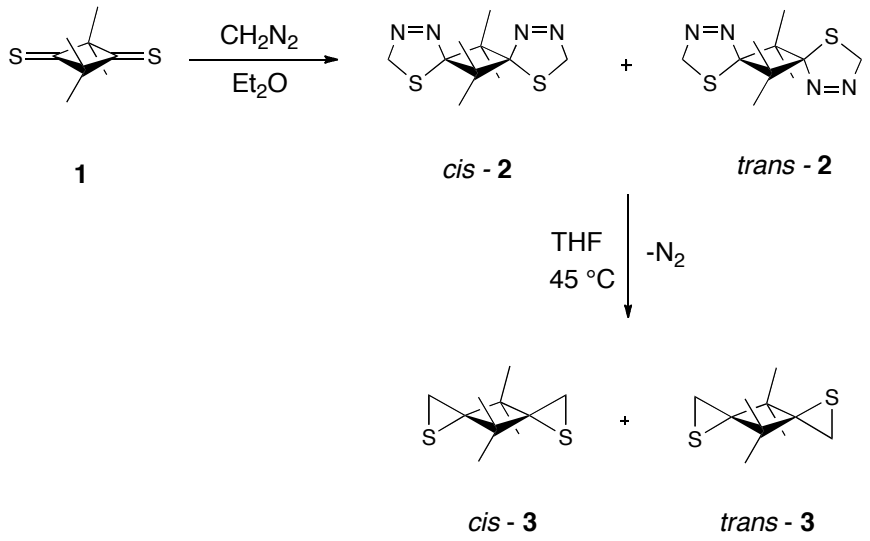
Thioketones are superior dipolarophiles, and they react smoothly with a variety of 1,3-dipoles to give the corresponding five-membered cycloadducts [1-3]. Reactions with diazomethane are of special interest, as the adducts, *i.e.* 2,5-dihydro-1,3,4-thiadiazoles, easily extrude N_2 to generate reactive thiocarbonyl *S*-methanides. In the last two decades,

* Authors for correspondence

these *in situ* generated 1,3-dipoles were studied extensively as useful building blocks for the synthesis of sulfur-containing compounds [4,5]. Attention is focused on their [2+3]-cycloadditions, which offer an access to five-membered S-heterocycles. Typical thiocarbonyl *S*-methanides are recognized as electron-rich 1,3-dipolar systems and react easily with electron-deficient dipolarophiles. In addition, reactions with C=S dipolarophiles occur very efficiently to yield 1,3-dithiolane derivatives (Schönberg reaction) [6].

Thionation of 2,2,4,4-tetramethylcyclobutane-1,3-dione yields a mixture of the corresponding mono- and dithione, which can easily be separated by column chromatography. Whereas the monothione has been used extensively as a favourite model of a cycloaliphatic C=S compound [7], dithione **1** has been applied less frequently [8,9]. Both thioketones react with diazomethane in a regioselective manner to give 2,5-dihydro-1,3,4-thiadiazoles, and in the case of **1**, a *ca.* 1:3 mixture of the bis-adducts *cis*- and *trans*-**2** is formed [10]. The separation of the two isomers by crystallization could not be achieved and, therefore, the mixture has been used for further reactions. Thermal decomposition of this mixture accompanied by elimination of N_2, carried out in the absence of trapping agents, yields a *ca.* 3:1 mixture of the bis-thiiranes *cis*- and *trans*-**3** (Scheme 1). Based on the knowledge of the mechanism of the reaction leading from 2,5-dihydro-1,3,4-thiadiazoles to thiiranes, thiocarbonyl ylides are accepted as being the key intermediates.

Scheme 1



In the present paper we describe first reactions of *cis*- and *trans*-**2** in which they are used as precursors of 'bis-thiocarbonyl ylides'.

RESULTS AND DISCUSSION

A solution of a recrystallized mixture of *cis*- and *trans*-**2** in THF was heated in the presence of two equivalents of *N*-methylmaleimide at 45°C. The reaction occurred with evolution of N_2, and after *ca*. 1 h, a colorless solid started to precipitate. When the evolution of N_2 ceased (3 h), the colorless solid was separated by filtration and identified as a bis-adduct (MS, elemental analysis). An additional crop of this material was obtained as the second fraction when the mother liquor was chromatographed (SiO_2). In the ^{1}H-NMR spectrum ($CDCl_3$), only one singlet for MeN and two singlets for MeC are present. The ^{13}C-NMR spectrum confirms the symmmetric structure of the molecule. Single crystals were obtained by crystallization from MeOH/CH_2Cl_2 (m.p. 305-307°C), and the structure of *cis-anti*-**4** (Scheme 2) was established by X-ray crystallography (Figure 1).

Scheme 2

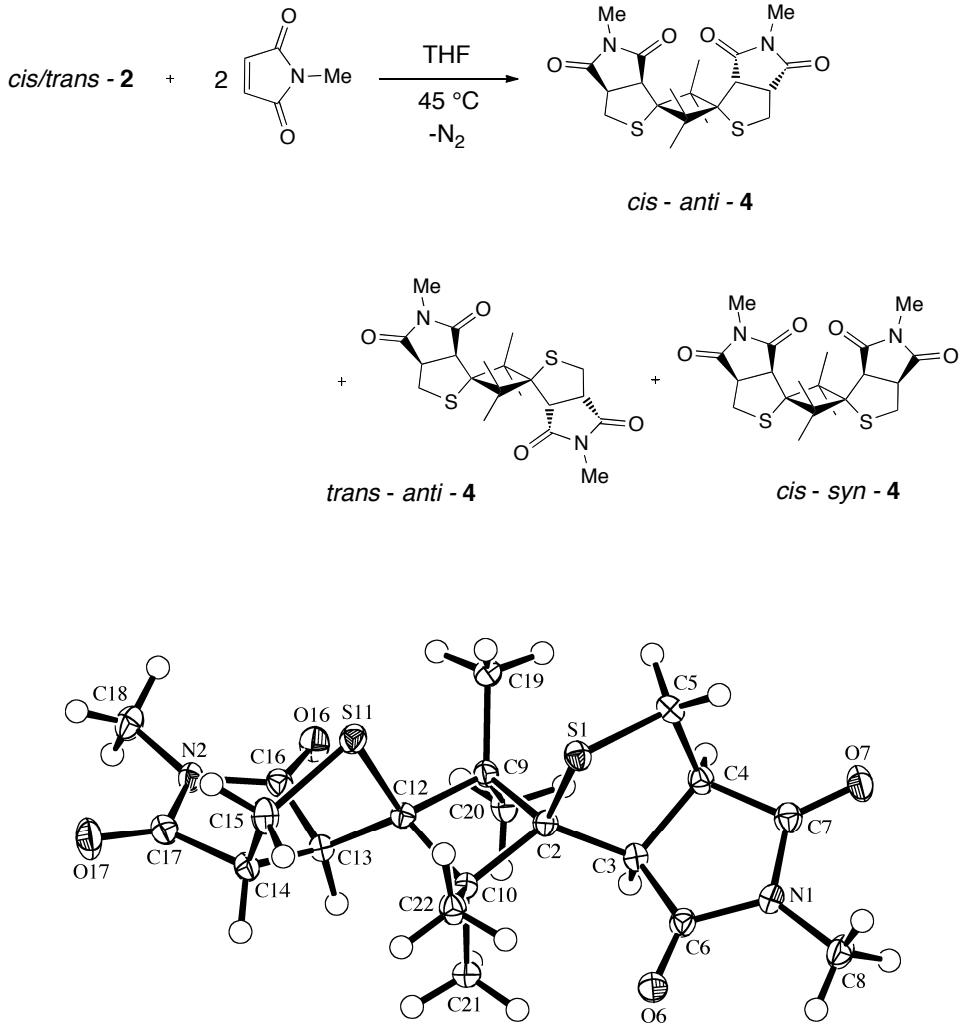


Figure 1. ORTEP-Plot [11] of the molecular structure of *cis-anti*-**4** (arbitrary numbering of the atoms; 50% probability ellipsoids)

Chromatographic separation of the mother liquor (SiO_2, CH_2Cl_2/MeOH) afforded three fractions, the second one being *cis-anti*-**4**. The first fraction also gave a crystalline product, which was recrystallized from MeOH/CH_2Cl_2 (m.p. 282-284°C). The MS and elemental analyses confirmed the molecular formula $C_{20}H_{26}N_2O_4S_2$, indicating that another bisadduct was obtained. The NMR spectra of this isomer were very similar to those of *cis-anti*-**4**. The structure of the expected *trans-anti*-**4** was confirmed by single-crystal X-ray crystallography (Figure 2).

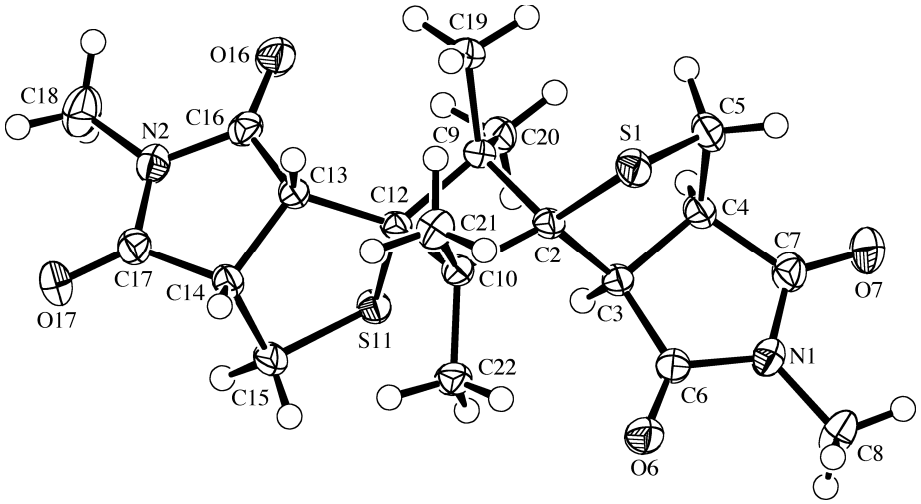


Figure 2. ORTEP-Plot [11] of the molecular structure of *trans-anti*-**4** (arbitrary numbering of the atoms; 50% probability ellipsoids)

Finally, a third crystalline isomer (m.p. 358-360°C) was isolated from the third fraction of the chromatography. The NMR spectra of this compound differed significantly from the previous ones, which indicated a less symmetric structure. The ^{1}H- and ^{13}C-NMR spectra showed four signals for the four MeC groups. The elucidation of the structure of *cis-syn*-**4** was again achieved by an X-ray crystal-structure determination (Figure 3).

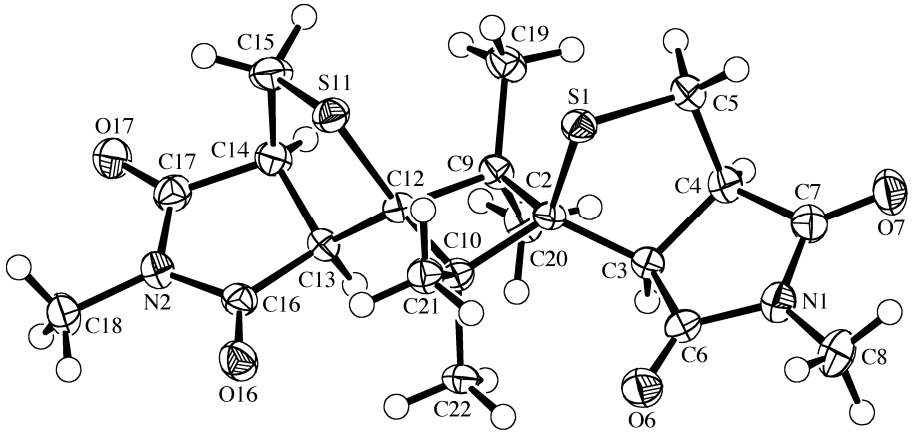
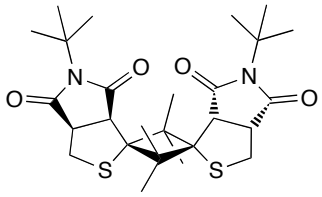


Figure 3. ORTEP-Plot [11] of the molecular structure of *cis-syn*-**4** (arbitrary numbering of the atoms; 50% probability ellipsoids)

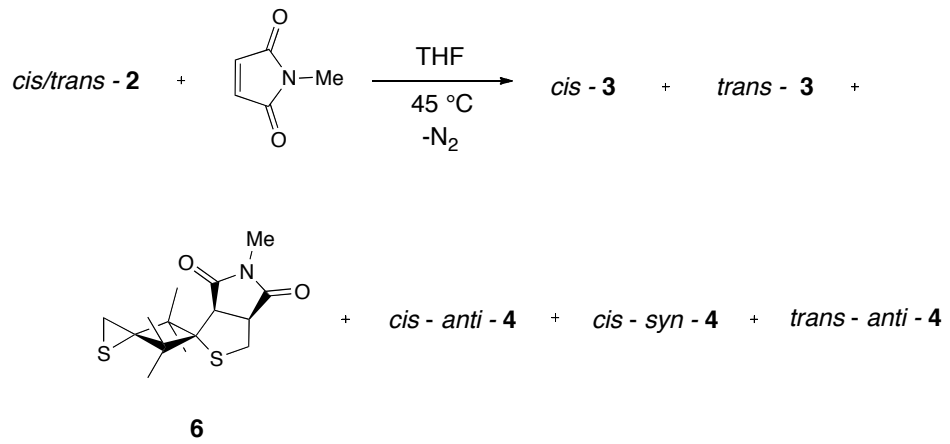
A similar result was obtained when *cis*/*trans*-**2** was decomposed in THF in the presence of two equivalents of *N*-(*tert*-butyl)maleimide. Also in this case, a colorless product precipitated from the solution, which, after isolation and purification, was identified as a bis-adduct. The high symmetry of the molecule revealed by the NMR data, together with its insolubility in THF, prompted us to propose the structure of *cis*-*anti*-**5**. The chromatographic separation of the mother liquor gave an additional amount of *cis*-*anti*-**5**, but the minor products could not be isolated.



cis - anti - **5**

In an analogous experiment, a solution of equimolar amounts of *cis*/*trans*-**2** and *N*-methylmaleimide was heated. As in the previous experiment, *cis*-*anti*-**4** was isolated as an insoluble solid, and subsequent chromatography of the mother liquor afforded, along with *trans*-*anti*-**4** and *cis*-*syn*-**4**, the known bis-thiiranes *cis*- and *trans*-**3**, plus a new product containing only one imide moiety. In the NMR spectra of the latter, four signals for MeC and one signal for MeN appear in equal intensity. Furthermore, an AB-system between 2 and 3 ppm can be attributed to a CH_2 group of a thiirane. Based on the spectroscopic data, a product **6** can be proposed in which the thiirane unit was formed by a 1,3-dipolar electrocyclization of an intermediate thiocarbonyl *S*-methanide. The bicyclic fragment of the molecule results from the [2+3]-cycloaddition of the thiocarbonyl *S*-methanide on the other side of the cyclobutane ring. The X-ray crystal structure determination confirmed the proposed structure and additionally established the *cis*-relationship of the two S-atoms (Figure 4).

Scheme 3



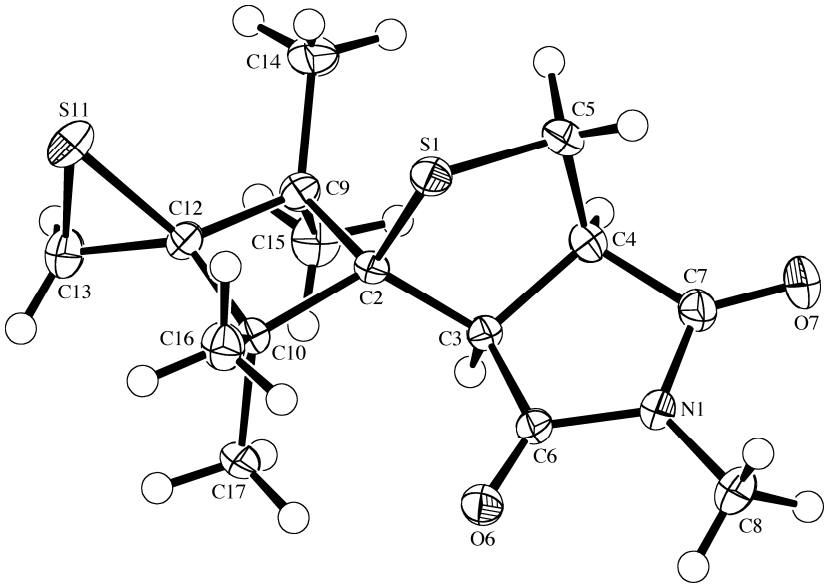


Figure 4. ORTEP-Plot [11] of the molecular structure of **6** (arbitrary numbering of the atoms; 50% probability ellipsoids)

In conclusion, the present study shows that the easily available mixture of *cis*- and *trans*-**2** can be used for the synthesis of fairly complex bis-spiroheterocycles in a one-pot procedure. The selectivity of the formation of the bis-adducts is rather low, but the *cis*-configured products dominate. It is most likely that the formation of the bis-adducts occur stepwise. The question as to whether the *cis*/*trans*-ratio of **2** determines the *cis*/*trans*-ratio of the products cannot be answered. The experiment with two equivalents of maleimide,

in which no thiirane formation was observed, shows that the [2+3]-cycloaddition of the intermediate thiocarbonyl *S*-methanide is faster than the 1,3-dipolar electrocyclization.

EXPERIMENTAL

1. General. For instruments and measurement techniques see [12]. The ^{13}C-NMR spectra were recorded by using DEPT registration.

2. Starting materials. 2,2,4,4-Tetramethylcyclobutane-1,3-dithione (**1**) was prepared according to [8] by thionation of commercially available 2,2,4,4-tetramethylcyclobutane-1,3-dione with P_2S_5 in pyridine at 110°C and subsequent chromatographic separation from the more polar 2,2,4,4-tetramethyl-3-thioxocyclobutanone on a SiO_2-packed column. *N*-Methylmaleimide was purchased (Sigma-Aldrich), and *N*-(*tert*-butyl)maleimide was prepared from maleic anhydride and *tert*-butylamine according to [13]. The mixture of *cis*- and *trans*-**2** (ca. 3:1) was prepared as a colorless solid by treatment of the dithione **1** with diazomethane in ether solution followed by crystallization of the crude material from pentane at –76°C [10].

3. Thermal decomposition of *cis*/*trans*-2 in the presence of *N*-methylmaleimide. 3.1. 1:2-Ratio of starting materials. A solution of *N*-methylmaleimide (721 mg, 6.5 mmol) and 768 mg (3 mmol) of a freshly recrystallized mixture of *cis*- and *trans*-**2** in abs. THF (2 ml) was placed in a round-bottom flask equipped with a magnetic stirring bar and connected with a gas-burette. The stirred solution was heated to 45°C (oil bath), and after 1 h, a colorless precipitate formed. After 3 h, the evolution of nitrogen ceased (ca. 70 ml, corresponding to ca. 93% of the expected amount). The mixture was cooled to room temperature and the colorless precipitate was filtered off (758 mg, m.p. 260-283°C). The mother liquor was evaporated to dryness and the semi-solid residue was crystallized from MeOH with small amounts of CH_2Cl_2. Next day, the colorless crystals (330 mg, m.p. 293-300°C) were filtered off. This material was combined with the previously separated solid and recrystallized from MeOH/CH_2Cl_2 yielding *cis*/*anti*-**4**. The

combined mother liquor was separated on PLC plates coated with SiO_2 using a mixture of CH_2Cl_2 and MeOH (98:2) as eluant. After repeated development (2x), three well separated fractions were obtained. They were identified as *trans-anti*-**4** (least polar fraction), *cis-anti*-**4** (additional amount), and *cis-syn*-**4**, respectively. All products were solid and purification was performed by fractional crystallization to yield analytically pure samples suitabel for X-ray crystal-structure determination. Reported yields refer to isolated products.

3.2. 1:1-Ratio of starting materials. A solution of *N*-methylmaleimide (333 mg, 3 mmol) and 768 mg (3 mmol) of a mixture of *cis*- and *trans*-**2** in abs. THF (2 ml) was treated according to the procedure described in section 3.1. After filtration of the precipitated *cis-anti*-**4**, the filtrate was separated chromatographically on PLC plates. A mixture of the bis-thiiranes *cis*- and *trans*-**3** was obtained as the least polar fraction, followed by thiirane **6** and three isomeric bis-adducts **4**. Analytically pure samples were obtained by fractional crystallization.

cis- *and* trans-*4,4,8,8-Tetramethyl-1,6-dithiadispiro[2.1.2.1]octane* (*cis*- and *trans*-**3**). Yield: 95 mg (16%), isolated as the least polar fraction of experiment 3.2. Colorless crystals. M.p. 200-206°C (hexane; [8]: m.p. 195-199 °C). IR (KBr): 2961*vs*, 1365*s*, 1119*m*, 1047*m*, 815*s*, 701*m*. ^{1}H-NMR (*cis*/*trans*-ratio 1:2): *cis*-**3**: 0.87 (*s*, 2 Me); 1.25 (*s*, 2 Me); 2.58 (*s*, 2 CH_2); *trans*-**3**: 1.05 (*s*, 4 Me); 2.58 (*s*, 2 CH_2).

cis-anti-*2′,2′,4′,4′,7,7″-Hexamethyldispiro[(3-thia-7-azabicyclo[3.3.0]octane}-2,1′-cyclobutane-3′,2″-(3-thia-7-azabicyclo[3.3.0]octane)]-6,6″,8,8″-tetrone* (*cis-anti*-**4**). Yield: 758 mg (60%), precipitated from the reaction mixture and isolated after PLC in experiment 3.1. Colorless crystals, m.p. 305-307°C (MeOH/CH_2Cl_2). IR (KBr): 1698*vs* (CO), 1432*s*, 1380*s*, 1303*m*, 1281*m*, 1038*m*. ^{1}H-NMR: 1.38 (*s*, 2 Me); 1.86 (*s*, 2 Me); 2.92 (*d*, *J* = 2.9 Hz, 2 H); 2.99 (*s*, 2 MeN); 3.21 (*m*, 4 H); 3.65 (*m*, 2 H). ^{13}C-NMR: 24.5 (2 Me); 24.6 (2 Me); 25.0 (2 MeN); 35.6 (2 CH_2); 45.3 (2 CH); 47.7 (2 C_q); 53.9 (2 CH); 71.3 (2 C_q); 175.8, 177.6 (2 CO). CI-MS (NH_3): 423 (100, $[M+1]^+$). Anal. Calc. for $C_{20}H_{26}N_2O_4S_2$ (422.57): C 56.85, H 6.20, N 6.63, S 15.18. Found: C 56.92, H 6.21, N 6.61, S 15.26.

trans-anti-*2′,2′,4′,4′,7,7″-Hexamethyldispiro[(3-thia-7-azabicyclo[3.3.0]octane}-2,1′-cyclobutane-3′,2″-(3-thia-7-azabicyclo[3.3.0]octane)]-6,6″,8,8″-tetrone* (*trans-anti*-

4). Yield: 150 mg (12%), isolated as the first fraction of the mother liquor in experiment 3.1 after PLC. Colorless crystals, m.p. 282-284°C (MeOH/CH_2Cl_2). IR (KBr): 1701*vs* (CO), 1432*s*, 1385*s*, 1302*m*, 1281*s*, 1031*m*. ^{1}H-NMR: 1.37 (*s*, 2 Me); 1.80 (*s*, 2 Me); 2.94 (*dd*, *J* = 12.8, 2.7 Hz, 2 H); 2.99 (*s*, 2 MeN); 3.17 (*dd*, *J* = 12.7, 10.2 Hz, 2 H); 3.34 (*m*, 2 H); 3.81 (*d*, *J* = 6.7 Hz, 2H). ^{13}C-NMR: 25.1 (2 MeN); 26.3 (2 Me); 27.4 (2 Me); 34.4 (2 CH_2); 47.3 (2 CH); 47.8 (2 C_q); 54.6 (2 CH); 72.3 (2 C_q); 175.4, 177.3 (2 CO). CI-MS (NH_3): 423 (100, $[M+1]^+$); EI-MS: 422 (<1, $M^{+\cdot}$), 211 (100), 196 (11), 126 (7), 111 (17). Anal. Calc. for $C_{20}H_{26}N_2O_4S_2$ (422.57): C 56.85, H 6.20, N 6.63, S 15.18. Found: C 56.70, H 6.46, N 6.57, S 14.98.

cis-syn-*2′,2′,4′,4′,7,7″-Hexamethyldispiro[(3-thia-7-azabicyclo[3.3.0]octane}-2,1′-cyclobutane-3′,2″-(3-thia-7-azabicyclo[3.3.0]octane)]-6,6″,8,8″-tetrone* (*cis-syn*-**4**). Yield: 130 mg (10%), isolated as the third fraction of the mother liquor in experiment 3.1 after PLC. Colorless crystals, m.p. 358-360°C (MeOH/CH_2Cl_2). IR (KBr): 1701*vs* (CO), 1435*s*, 1380*m*, 1302*m*, 1281*s*, 1159*m*, 1038*m*. ^{1}H-NMR: 1.36, 1.44, 1.48, 2.26 (4*s*, 4 Me); 2.93 (*dd*, *J* = 12.6, 2.6 Hz, 2 H); 2.99 (*s*, 2 MeN); 3.23 (*m*, 2 H); 3.34 (*dd*, *J* = 12.5, 10.8 Hz, 2 H); 3.59 (*d*, *J* = 6.3 Hz, 2H). ^{13}C-NMR: 23.6, 24.5, 25.3, 26.2 (4 Me); 25.0 (2 MeN); 35.8 (2 CH_2); 44.3 (1 C_q); 46.1 (2 CH); 49.3 (1 C_q); 54.1 (2 CH); 71.5 (2 C_q); 175.5, 177.4 (2 CO). CI-MS (NH_3): 423 (100, $[M+1]^+$); EI-MS: 422 (<1, $M^{+\cdot}$), 211 (100), 196 (11), 126 (7), 111 (17). Anal. Calc. for $C_{20}H_{26}N_2O_4S_2$ (422.57): C 56.85, H 6.20, N 6.63, S 15.18. Found: C 56.67, H 6.37, N 6.58, S 14.98.

cis-*2′,2′,4′,4′,7″-Pentamethyldispiro[thiirane-2,1′-cyclobutane-3′,2″-(3-thia-7-aza-bicyclo[3.3.0]octane)]-6″,8″-dione* (**6**). Yield: 210 mg (22%), isolated as the second fraction of the mother liquor in experiment 3.2 after PLC. Colorless crystals, m.p. 164-166°C (MeOH/CH_2Cl_2). IR (KBr): 2958*m*, 1702*vs* (CO), 1436*s*, 1379*m*, 1301*m*, 1281*m*, 1037*m*. ^{1}H-NMR: 1.10, 1.19, 1.35, 1.71 (4*s*, 4 Me); 2.28, 2.36 (*AB*, *J* = 14.5 Hz, 2 H thiirane); 3.00 (*s*, MeN); 2.95, 3.17, 3.32 (3*m*, 3 H); 3.72 (*d*, *J* = 6.7 Hz, 1 H). ^{13}C-NMR: 22.2 (CH_2 thiirane); 24.9 (MeN); 25.0, 25.9, 26.2, 27.8 (4 Me); 34.9 (CH_2 thiophene); 44.2 (1 C_q); 46.6, 46.7, 53.6 (3 CH); 64.2 (1 C_q); 175.8, 177.6 (2 CO). CI-MS (NH_3): 329 (<1, $[M+NH_4]^+$), 312 (2, $[M+1]^+$), 311 (47, $M^{+\cdot}$). Anal. Calc. for $C_{15}H_{21}NO_2S_2$ (311.47): C 57.84, H 6.79, N 4.50, S 20.59. Found: C 58.22, H 7.13, N 4.49, S 20.80.

4. Thermal decomposition of *cis*/*trans*-2 in the presence of *N*-(*tert*-butyl)maleimide. A solution of *N*-(*tert*-butyl)maleimide (306 mg, 2 mmol) and 259 mg (1 mmol) of *cis*/*trans*-**2** in abs. THF (1 ml) was treated as described in section 3.1. A colorless precipitate formed after 1 h; the reaction was complete after 3 h. The colorless solid was filtered, and the mother liquor was chromatographed on PLC plates. The second fraction was combined with the filtered material and crystallized from MeOH with small amounts of CH_2Cl_2 yielding 215 mg (42%) of crude *cis-anti*-**5**. This material was recrystallized from MeOH/CH_2Cl_2 to give analytically pure *cis-anti*-**5**.

cis-anti-*2′,2′,4′,4′-Tetramethyl-7,7″-di*(tert-*butyl)dispiro[(3-thia-7-azabicyclo-[3.3.0]octane}-2,1′-cyclobutane-3′,2″-(3-thia-7-azabicyclo[3.3.0]octane)]-6,6″,8,8″-tetrone* (*cis-anti*-**5**). Yield: 123 mg (24%). Colorless crystals, m.p. 326-328°C (MeOH/CH_2Cl_2). IR (KBr): 1702*vs* (CO), 1341*s*, 1265*m*, 1182*m*, 1121*m*. ^{1}H-NMR: 1.36 (*s*, 2 Me); 1.56 (*s*, 6 Me); 1.79 (*s*, 2 Me); 2.87 (*dd*, *J* = 12.7, 2.6, 2 H); 2.95-3.02 (*m*, 2 H); 3.22 (*dd*, *J* = 12.6, 10.4, 2 H); 3.49 (*d*, J = 6.7, 2 H). ^{13}C-NMR: 24.6 (2 Me); 24.7 (2 Me); 28.3 (6 Me); 35.0 (2 CH_2); 45.4 (2 CH); 47.8 (2 C_q); 53.7 (2 CH); 58.4 (2 C_q); 72.1 (2 C_q); 176.5, 178.7 (2 CO). CI-MS (i-C_4H_{10}): 507 (100, $[M+1]^+$). Anal. Calc. for $C_{26}H_{38}N_2O_4S_2$ (506.73): C 61.63, H 7.56, N 5.53, S 12.66. Found: C 61.31, H 7.40, N 5.62, S 12.31.

5. *X-Ray Crystal-Structure Determination of* cis-anti-**4**, trans-anti-**4**, cis-syn-**4**, *and* **6** (see Table 1 and Figs. 1-4)*. All measurements were made on a *Nonius KappaCCD* diffractometer [14] using graphite-monochromated MoK_α radiation (λ 0.71073 Å) and an *Oxford Cryosystems Cryostream 700* cooler. Data reduction was performed with *HKL Denzo* and *Scalepack* [15]. The intensities were corrected for *Lorentz* and polarization effects, and in each case, an absorption correction based on the multi-scan method [16] was applied. Equivalent reflections were merged. Data collection and refinement

---

* CCDC-238158–CCDC-238161 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge *via* www.ccdc.cam.ac.uk/conts/retrieving.html (or from the *Cambridge Crystallographic Data Centre*, 12 Union Road, Cambridge CB2 1EZ, U.K.; fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk).

parameters are given in Table 1, and views of the molecules are shown in Figs. 1-4. The structures were solved by direct methods using SIR92 [17], which revealed the positions of all non-H-atoms, and the non-H-atoms were refined anisotropically. In the case of *cis-anti*-**4**, the asymmetric unit contains one molecule of the bis-adduct plus one MeOH molecule. The hydroxy H-atom of the MeOH molecule was placed in the position indicated by a difference electron density map and its position was allowed to refine together with an isotropic displacement parameter. All remaining H-atoms and all of the H-atoms of *cis-syn*-**4**, *trans-anti*-**4** and **6**, were placed in geometrically calculated positions and refined using a riding model where each H-atom was assigned a fixed isotropic displacement parameter with a value equal to $1.2U_{eq}$ of its parent C-atom ($1.5U_{eq}$ for the Me groups). Refinement of each structure was carried out on F^2 using full-matrix least-squares procedures, which minimized the function $\Sigma w(F_o^2-F_c^2)^2$. A correction for secondary extinction was applied in each case. Neutral atom scattering factors for non-H-atoms were taken from [18a], and the scattering factors for H-atoms were taken from [19]. Anomalous dispersion effects were included in F_c [20]; the values for f' and f'' were those of [18b]. The values of the mass attenuation coefficients are those of [18c]. All calculations were performed using the SHELXL97 [21] program.

Acknowledgement

We thank the analytical services of our institutes for spectra and analyses, and the *Polish State Committee for Scientific Research* (Grant No. 4 T09A 046 25) and *F. Hoffmann-La Roche AG,* Basel, for financial support. Some preliminary experiments were carried out by *E. Janicka* within her diploma thesis, University of Lodz, 2001

Table 1. *Crystallographic Data of* cis-anti-**4**, cis-syn-**4**, trans-anti-**4** and **6**

		cis-anti-**4**	*cis-syn*-**4**
Crystallized from		MeOH / CH_2Cl_2	MeOH / CH_2Cl_2
Empirical formula		$C_{20}H_{26}N_2O_4S_2 \cdot CH_3OH$	$C_{20}H_{26}N_2O_4S_2$
Formula weight [g mol^{-1}]		454.60	422.55
Crystal color, habit		colorless, prism	colorless, prism
Crystal dimensions [mm]		0.20 × 0.22 × 0.25	0.10 × 0.15 × 0.20
Temperature [K]		160(1)	160(1)
Crystal system		monoclinic	monoclinic
Space group		$P2_1/c$	$P2_1/n$
Z		4	4
Reflections for cell determination		24744	14321
2θ range for cell determination [°]		4–55	4–50
Unit cell parameters	a [Å]	9.9401(1)	8.8947(2)
	b [Å]	15.0102(2)	19.8373(5)
	c [Å]	14.4771(2)	11.4614(3)
	β [°]	102.2342(6)	101.553(1)
	V [Å^3]	2110.97(5)	1981.36(9)
D_X [g cm^{-3}]		1.430	1.416
μ(Mo $K\alpha$) [mm^{-1}]		0.289	0.299
Scan type		ϕ and ω	ϕ and ω
$2\theta_{(max)}$ [°]		55	50
Transmission factors (min; max)		0.580; 0.949	0.904; 0.973
Total reflections measured		47295	28398
Symmetry independent reflections		4831	3507
Reflections with $I > 2\sigma(I)$		3913	2573
Reflections used in refinement		4831	3507
Parameters refined		283	260
Final $R(F)$ [$I>2\sigma(I)$ reflections]		0.0378	0.0442
$wR(F^2)$ (all data)		0.1012	0.1167
Weights: $w = [\sigma^2(F_o^2) + (0.0507P)^2 + 1.0883P]^{-1}$ where $P = (F_o^2 + 2F_c^2)/3$			$w = [\sigma^2(F_o^2) + (0.0595P)^2 + 0.4849P]^{-1}$
Goodness of fit		1.036	1.045

Secondary extinction coefficient	0.004(1)	0.004(1)
Final Δ_{max}/σ	0.001	0.001
$\Delta\rho$ (max; min) [e Å^{-3}]	0.37; -0.31	0.41; -0.39

Table 1. *Crystallographic Data of* cis-anti-**4**, cis-syn-**4**, trans-anti-**4** and **6** (continued)

		trans-anti-**4**	**6**
Crystallized from		MeOH / CH_2Cl_2	MeOH / CH_2Cl_2
Empirical formula		$C_{20}H_{26}N_2O_4S_2$	$C_{15}H_{21}NO_2S_2$
Formula weight [g mol^{-1}]		422.55	311.46
Crystal color, habit		colorless, plate	colorless, prism
Crystal dimensions [mm]		0.05 × 0.22 × 0.25	0.22 × 0.22 × 0.30
Temperature [K]		160(1)	160(1)
Crystal system		monoclinic	monoclinic
Space group		$P2_1/n$	$C2/c$
Z		4	8
Reflections for cell determination		23931	24244
2θ range for cell determination [°]		4–55	4–60
Unit cell parameters	a [Å]	13.3355(2)	28.0503(3)
	b [Å]	10.8632(2)	7.4337(1)
	c [Å]	14.5893(2)	15.6802(2)
	β [°]	111.8998(9)	108.6450(5)
	V [Å^3]	1960.98(6)	3098.00(7)
D_x [g cm^{-3}]		1.431	1.335
μ(Mo $K\alpha$) [mm^{-1}]		0.302	0.344
Scan type		ϕ and ω	ϕ and ω
2θ(max) [°]		55	60
Transmission factors (min; max)		0.924; 0.987	0.830; 0.929
Total reflections measured		44431	47604
Symmetry independent reflections		4498	4531
Reflections with $I > 2\sigma(I)$		3460	3632
Reflections used in refinement		4498	4531
Parameters refined		260	187
Final $R(F)$ [$I>2\sigma(I)$ reflections]		0.0392	0.0376

$wR(F^2)$ (all data)	0.1033	0.1008
Weights: $w = [\sigma^2(F_o^2) + (0.0506P)^2 + 0.6143P]^{-1}$		$w = [\sigma^2(F_o^2) + (0.0478P)^2 + 2.4344P]^{-1}$
where $P = (F_o^2 + 2F_c^2)/3$		
Goodness of fit	1.065	1.056
Secondary extinction coefficient	0.0044(9)	0.0017(3)
Final Δ_{max}/σ	0.001	0.001
$\Delta\rho$ (max; min) [e Å^{-3}]	0.29; -0.34	0.43; -0.35

REFERENCES

[1] Huisgen R., Li X., Giera H. and Langhals E., *Helv. Chim. Acta*, **84**, 981 (2001).

[2] Huisgen R. and Mloston G., *Pol. J. Chem.*, **73**, 635 (1999).

[3] Okuma K., *Sulfur Rep.* **23**, 209 (2002).

[4] Mloston G. and Heimgartner H., *Pol. J. Chem.,* **74**, 1503 (2000).

[5] Mloston G. and Heimgartner H., in "The Chemistry of Heterocyclic Compounds, Vol. 59: Synthetic Applications of 1,3-Dipolar Cycloaddition Chemistry Toward Heterocycles and Natural Products", Eds. Padwa A. and Pearson W.H., J. Wiley & Sons, New York, 2002, p. 315.

[6] Huisgen R., Kalwinsch I., Li X. and Mloston G., *Eur. J. Org. Chem.*, 1685 (2000).

[7] Heimgartner H. and Mloston G., in ‚Electronic Encyclopedia of Reagents in Organic Synthesis', Eds. Paquette L., Rigby J., Crich D. and Wipf P., John Wiley & Sons, Chichester, West Sussex, PO19 8SQ, UK, Article RN00429.

[8] Krapcho A.P., Rao D.R., Silvon M.P. and Abegaz B., *J. Org. Chem.*, **36**, 3885 (1971).

[9] Heimgartner H. and Mloston G., in ‚Electronic Encyclopedia of Reagents in Organic Synthesis', Eds. Paquette L., Rigby J., Crich D. and Wipf P., John Wiley & Sons, Chichester, West Sussex, PO19 8SQ, UK, Article RN00430.

[10] Mloston G., Romanski J., Linden A. and Heimgartner H., *Helv. Chim. Acta*, **80**, 230 (1997).

[11] Johnson C.K., 'ORTEP II', Report ORNL-5138, Oak Ridge National Laboratory, Oak Ridge, Tennessee, 1976.

[12] Mloston G., Romanski J. and Heimgartner H., *Pol. J. Chem.*, **75**, 975 (2001).

[13] Wang Z. Y., *Synth. Commun.* **20**, 1607 (1990).

[14] Hooft R., *KappaCCD Collect Software*, Nonius BV, Delft, The Netherlands, 1999.

[15] Otwinowski Z. and Minor W., in 'Methods in Enzymology', Vol. 276, 'Macromolecular Crystallography', Part A, Eds. Carter C.W., Jr. and Sweet R.M., Academic Press, New York, 1997, p. 307.

[16] Blessing R.H., *Acta Crystallogr., Sect. A*, **51**, 33 (1995).

[17] Altomare A., Cascarano G., Giacovazzo C., Guagliardi A., Burla M.C., Polidori G. and Camalli M., SIR92, *J. Appl. Crystallogr.*, **27**, 435 (1994).

[18] a) Maslen E.N., Fox A.G. and O'Keefe M.A., in 'International Tables for Crystallography', Ed. Wilson A.J.C., Kluwer Academic Publishers, Dordrecht, 1992, Vol. C, Table 6.1.1.1, p. 477; b) Creagh D.C. and McAuley W.J., *ibid.* Table 4.2.6.8, p. 219; c) Creagh D.C. and Hubbell J.H., *ibid.* Table 4.2.4.3, p. 200.

[19] Stewart R.F., Davidson E.R. and Simpson W.T., *J. Chem. Phys.*, **42**, 3175 (1965).

[20] Ibers J.A. and Hamilton W.C., *Acta Crystallogr.* **17**, 781 (1964).

[21] Sheldrick G.M., SHELXL97, Program for the Refinement of Crystal Structures, University of Göttingen, Germany, 1997.